

### **REMARKS**

To facilitate consideration, Applicants have amended the case to cancel withdrawn claims 1-7 and 16-52. Moreover, the pursuant to the Examiner's suggestion, claim 8 has been made independent, and further recites the features of originally advanced claim 27, wherein the dendrimer further bears, in addition to the dioxetane chemiluminescent moiety conjugated to the dendrimer, a plurality of enhancer moieties effective to increase the intensity of light released by the substrate delivery system upon triggering of the dioxetane moieties. This invention is also disclosed in the application, as originally filed, see page 26, line 10 – page 29, line 14 of the specification. Accordingly, the claims have been amended to combine them to elected subject matter, and further amended, without the addition of new matter, to more clearly and carefully reflect the invention. Upon entry, claims 8-15 remain pending in the file. Entry is respectfully requested.

### **REQUEST FOR RECONSIDERATION**

All claims pending stand rejected over at least U.S. Patent 5,338,532, taken in combination with what the Examiner as “admitted prior art as set forth at page 6 of the instant specification” (Office Action, page 2, item 4) further in view of Simons. It is the apparent position of the Examiner that the principle reference, Tomalia describes dendrimers “with a wide variety of detectable moieties including optically detectable moieties” and that accordingly, the dioxetanes of the claimed substrate delivery system would be obvious substitutes. The Examiner particularly notes that they would be obvious in view of their prior art recognition as optically detectable, see page 6 of the specification. The rejection is respectfully traversed.

Initially, Applicants respectfully submit that the Examiner has read Tomalia too broadly. Tomalia does not describe the combination of a dendrimer with virtually any “optically detectable” moiety attached thereto. Rather, Tomalia specifically teaches the preparation of dendrimers with bioactive agents attached thereto. Column 1, lines 39-45. No other embodiment is described. In the Office Action of February, 2005, the Examiner drew specific attention to portions of the specification of Tomalia. Specifically, the Examiner cited to column 6, line 61 – column 7, line 20; column 8, lines 32-35; column 4, lines 48 – column 5, line 35; column 12, line 54 – column 13, line 28 and column 15, lines 15-50. Respectfully, none of the citations suggest the combination of a dendrimer and a dioxetane, or any chemiluminescent substrate of any type. The Examiner has read Tomalia in light of Applicants’ specification, impermissible hindsight in presenting a rejection under 35 U.S.C. § 103.

Turning first to column 6, line 61 – column 7, line 20, it is in fact true that the reference discloses an unbelievable number of possible combinations for the dendrimer. Each of these, the reference represents the dendrimer with “at least one carried agricultural, pharmaceutical, or other material.” Column 6, line 63-64. The reference provides additional teachings as to what these materials can be. Column 7, line 9, the reference identifies the carried material as a “bioactive agent.” In several different places, the reference identifies possibilities for the “carried material” as “a drug, pesticide, radionuclide, chelant, chelated metal, toxin, antibody, antibody fragment, antigen” see column 7, lines 13-16. The closest the references comes to the claimed invention is the suggestion of a signal generator. It identifies “fluorescing entities, signal reflector, for example, paramagnetic entities, or signal absorber, for example, electron beam opacifiers, fragrance, pheromones, or dyes.” This disclosure appears at column 7, line 16-20, and in more detail, column 8, lines 32-45. Again, the identified “signal generators” are

identified as fluorescent entities, opacifiers and in particular, pharmaceutical agents. None of these describe dioxetanes. Dioxetanes do not fluoresce, they are chemiluminescent. One can search the entirety of Tomalia, and find no reference to chemiluminescent emitters. They are, in particular, not bioactive agents. The rest of Tomalia is to the same effect.

With respect to the citation at column 8, line 32-35, again, the reference describes fluorescing entities, phosphorescence entities and radiation. None of these are dioxetanes. The other citations offered by the Examiner are equally inapt. The Examiner directs attention to column 4, line 48 – column 5, line 35. Column 4, line 48 describes the dendrimer itself, it merely describes them as “targeted carriers of bioactive agents capable of delivering the bioactive agents to a particular target organism or a particular determinant or locus in a target organism.” Dioxetanes are not bioactive agents, and a starburst dendrimer coupled to dioxetanes without more are not “capable of delivering bioactive agents to a particular target organism.” Column 12 does not further teach the invention. Column 12, line 54 – column 13 of Tomalia, there are described embodiments, when “the carried materials are pharmaceutical materials.” Column 12, lines 54-55. The disclosure also embraces previously disclosed signal generators. As one can see from the Tomalia disclosure itself, there are literally thousands of potential signal generators. More is required by way of disclosure to lead one of skill in the art to combine the dendrimers of Tomalia with the dioxetanes of the prior art. Column 15, lines 15-50 simply describes a variety of linking agents, and not the dioxetane-substituted dendrimers of the claimed invention. It is Applicants, not the prior art, who have suggested the combination of dendrimers with dioxetanes.

Applicants respectfully request the Examiner point with specificity to that aspect of the prior art, the patents that describe dioxetanes or the Tomalia patent, that would lead of skill in the

art to combine the two. Indeed, it seems evident that Tomalia never envisioned the use of chemiluminescent substrates such as dioxetanes.

Beyond the simple failing of the art to teach the combination claimed herein, without some specific direction to that end, Applicants have amended the claims herein to reflect that the dendrimer supports not only the dioxetane moieties recited but enhancement groups. While ordinarily, the dioxetanes of the prior art have been used either in hydrophobic microenvironments formed in solution, or on surfaces tending to exclude water, Applicants have developed large substrate delivery systems which provide their own hydrophobic environment, allowing an increase in intensity of light release, over the use of the dioxetanes alone. This is certainly nowhere suggested in the art.

Applicants further note that the combination of dioxetanes with dendrimers leads to an advantage not recognized or observed in the art. The dendrimer itself provides a unique environment hospitable to the release of light, which is quenched by the presence of water. See in particular, page 10 of the application, which discusses the improvement of signal resolution from chemiluminescent substrates due to their presence on the dendrimer alone without further enhancement. The dendrimer itself offers an enhancing region, even in the absence of specific coupling of the enhancing moieties of the claimed invention. See page 10, lines 18-25. This advantage is discussed in detail at page 11, lines 1-15. Nothing in the art suggests improvement in light intensity release by the coupling of dioxetanes to dendrimers, without more. Thus, not only is the claimed invention untaught by the prior art, but it results in a unique advantage, enhanced light intensity, simply by the coaction of the dioxetane and the dendrimer, a coaction not previously taught. When this enhancement effect is coupled with the placement of the

polymeric ammonium salt or albumin recited in the claims, a truly different and unobvious invention is provided.

Should the Examiner elect to persist in the rejection, the Examiner is respectfully indicated to point to that aspect of Tomalia that specifically teaches the use of chemiluminescent compounds, and in particular, dioxetanes, in combination with dendrimers, as well as the unique properties thereof. Further, Applicants respectfully require the Examiner indicate where the principle reference teaches the simultaneous attachment of light intensity enhancement agents, such as those recited in the claims.

Applicants have canceled all withdrawn claims for the purposes of advancing prosecution. Neither the attachment of chemiluminescent dioxetanes to the dendrimers of the claimed invention, nor the further improvement of the provision of enhancement agents on the dendrimer to further increase light intensity is suggested by the prior art. Accordingly, the claims are directed to allowable subject matter and an early and favorable Office Action thereon is respectfully requested.

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Date

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